Clinical Pharmacist Impact on Intensive Care Unit Delirium: Intervention and Monitoring

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Abstract

Purpose: The purpose of this study was to determine the impact of pharmacist monitoring with a clinical decision support system (CDSS) on clinical outcomes related to intensive care unit (ICU) delirium. **Methods:** This was a single-center, before-and-after study. This study compares patient outcomes of the preintervention group, which is the standard of care of pharmacist rounding, and the intervention group of pharmacy rounding with the CDSS rules. Using a CDSS, specific delirium risk factor rules were created to alert pharmacists to patients who have an increased risk of developing ICU delirium. Patients were included in the study if they were ≥ 18 years of age, admitted to the trauma intensive care unit (TICU), and had one of the CDSS rule alerts. The CDSS notified pharmacists in real time to patients in the intervention group that met these criteria to provide timely recommendations in an effort to prevent ICU delirium. **Results:** Compared with the preintervention group receiving the standard of care ($n = 28$), the intervention CDSS group ($n = 33$) had a nonsignificant trend in decreased incidence of delirium (33.3% vs 24.1%, $P = .45$), ICU length of stay (LOS) (10.11 vs 7.55 days, $P = .26$), and ventilator duration (7.11 vs 5.03 days, $P = .26$). The intervention group had a significantly shorter hospital LOS (14.74 vs 9.98 days, $P = .04$). There was a nonsignificant increase in mortality with the intervention group from nondelirium causes (24.2% vs 7%, $P = .07$). **Conclusion:** The utilization of a CDSS by clinical pharmacists to monitor for delirium-specific risk factors led to a significantly shorter hospital LOS. Further studies using this model are warranted to see the impact on the ICU population.

Keywords

ICU delirium, delirium, benzodiazepines, pharmacists, sedation, CDSS, clinical decision support system

Introduction

Delirium is an insidious cognitive dysfunction which can lead to deleterious clinical outcomes such as death and accelerated cognitive decline.¹ This acute cognitive dysfunction has also been associated with an annual health care cost of \$4 to \$16 billion in the United States alone.² Unfortunately, delirium commonly occurs in elderly patients during hospitalization and has been estimated to occur in up to 80% of mechanically ventilated adult intensive care unit (ICU) patients.^{2,3} Delirium is an independent risk factor for increased mortality within 12 months after hospitalization and is associated with increased length of ICU stay, increased hospital acquired infections, and persistent cognitive deficits.^{4,5}

Many different risk factors have been attributed to the development of delirium, some of which are modifiable such as sedatives, benzodiazepines, anticholinergics, opioids, and environmental conditions.² The ICU delirium may be preventable with routine monitoring, yet often goes undiagnosed due to a lack of screening and mismanagement of the modifiable risk factors. Institutions that have developed ICU delirium protocols or provided education have demonstrated significant reductions in the incidence of delirium, hospital length of stay (LOS), and improved patient outcomes.^{6,7,8}

Clinical decision support systems (CDSS) are being increasingly utilized by pharmacists and other health care professionals to receive timely clinical information, efficiently monitor patients, and provide appropriate care. Facilities that have implemented CDSS have documented an increase in clinical interventions from an average of 1986 per month to 4065 per month.⁹ The CDSS may not only increase quality patient care but also increase communication among providers. A study by Calloway et al demonstrated an annual cost savings of \$3 million when patient care teams utilized CDSS. The CDSS used by pharmacists allows the creation of meaningful rules that alert the pharmacists in real time. This affords pharmacists the opportunity to respond in a timely manner to improve patient care and increase medication safety. The goal of this study was to determine whether clinical pharmacists utilizing a CDSS for monitoring sedatives and psychotropic medications related to delirium risk factors in the trauma intensive care unit (TICU) would decrease the incidence of delirium.

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Materials and Methods

This was a single-center, before-and-after study conducted at Tristar Skyline Medical Center in Nashville, Tennessee. Using a CDSS, specific medication-related delirium risk factor rules were created to alert pharmacists to patients who have increased risk(s) of developing ICU delirium. With CDSS, clinical pharmacists were alerted to a patient who met specific risk factors for developing ICU delirium in our institution in real time. Recommendations were made in accordance to the standard of care from the 2013 Society of Critical Care Medicine's Pain, Agitation, and Delirium guidelines.² The CDSS rules included patients on continuous sedation, ≥ 2 anticholinergic agents for patients 65 years of age and older, ≥ 2 antipsychotics, ≥ 2 benzodiazepines, and administration of ≥ 12 mg of lorazepam equivalents of benzodiazepines in 2 hours (Table 1). The CDSS searches were completed daily for continuous sedation, using barcode medication administration (BCMA) data to capture patients to be included in the current study. Continuous sedation medication included lorazepam, fentanyl, propofol and dexmedetomidine. Institutional review board (IRB) approval was obtained and informed consent was waived.

Inclusion criteria were defined as patients ≥ 18 years of age, admitted to the TICU, and a minimum of one delirium-specific CDSS alert or identification of continuous sedation from a CDSS search. The study took place over 90 days from January 1, 2017, through March 31, 2017. Real time alerts for pharmacist monitoring of the CDSS rules began on February 15, 2017. Patients who met this criterion prior to the implementation of CDSS rules (preintervention group) were compared with those who developed it following delirium-specific CDSS pharmacist monitoring (intervention group). Patients meeting inclusion criteria between January 1 and February 14, 2017 (45 days) were in the preintervention group and patients were included in the intervention group that met inclusion criteria from February 15 to March 31, 2017 (45 days). Patients were included in the intervention group if they were admitted prior to February 15, but did not meet inclusion criteria until after the deployment of the CDSS rules. Patients were excluded from the study if they qualified to be in the preintervention group and had CDSS alerts during the intervention phase. In the preintervention group, a clinical pharmacist accompanied the daily rounds with the multidisciplinary team, where they would work up and discuss ICU delirium risk factors during rounds. Whereas in the intervention group, the clinical pharmacist rounded and was alerted by the CDSS throughout the entirety of their shift to potential delirium-potentiating, drug-related issues.

Depth of sedation was assessed using the Richmond Agitation Sedation Scale (RASS). Nurses were required to document all RASS scores and infusion rates of sedation medications on the electronic medication record. Delirium was assessed using the Confusion Assessment Method for Intensive Care Unit (CAM-ICU) score and was documented by nurses in the patient's medical record by either stating "delirium" or

Table 1. Benzodiazepine Conversion Chart.^{10,11}

Benzodiazepine	Converted lorazepam equivalents (mg)
Alprazolam	0.5
Chlordiazepoxide	25
Clonazepam	0.25
Diazepam	5
Lorazepam	1
Midazolam	3
Oxazepam	15
Temazepam	10

"no delirium." A retrospective data search utilizing the CDSS was performed for the time frame covering the preintervention group and determined which patients met inclusion criteria based on the delirium-specific CDSS alerts that would have occurred. A daily report was performed utilizing the CDSS to identify patients admitted to the TICU on continuous sedation during the intervention phase. Pharmacists involved in the study participated in daily multidisciplinary trauma rounds and monitored TICU patients on a daily basis. During the intervention period, pharmacists were given a standard recommendation algorithm (see the appendix) for the new delirium-specific CDSS alerts. Clinical pharmacists involved in the current study utilized CDSS for real-time alerts for delirium modifiable risk factors and would make recommendations during multidisciplinary rounds using their clinical judgment. All recommendations and other pharmaceutical interventions were documented in the CDSS.

The primary endpoint was occurrence of ICU delirium, measured by a CAM-ICU score showing the presence of delirium. Secondary endpoints included hospital LOS (days), ICU LOS (days), ventilator duration (days), and delirium-potentiating medications administered to patients. For all trauma admissions patients, a trauma and injury severity score (TRISS) was calculated, which determines the probability of survival. On admission, all TICU patients also received an alcohol score by the CAGE questionnaire. The CAGE questionnaire is a screening tool to determine whether a patient has a potential alcohol problem. The CAGE questionnaire asks the following questions: Have you ever felt you should Cut down on your drinking?; Have people Annoyed you by criticizing your drinking?; Have you ever felt bad or Guilty about your drinking?; Have you ever had a drink first thing in the morning to steady your nerves or to get rid of a hangover (Eye opener)? Responses are scored 0 or 1, higher the score indicates an alcohol problem.¹²

The chi-square test was used to compare the preintervention and intervention groups to assess the nominal data, and the *t* test was used to assess all continuous variables. Continuous data, such as the TRISS scores, were transformed by log transformation of the inverse of the values to remove substantial negative skewness in the data to get it closer to a normal distribution. The *N* needed for a two-sample *t* test was 64 in each group for 80% power. For all statistical tests, *P* < .05 was considered to be significant.

Table 2. Patient Characteristics.

	Preintervention (n = 28)	Intervention (n = 33)	P value
Gender			
Male	18 (64%)	22 (66%)	0.17
Average age, years	47	54	0.19
Patients ≥ 65 , years	5 (18%)	10 (31%)	0.17
Age-minimum	26	19	NA
Age-maximum	76	88	NA
CIWA protocol	6 (21.4%)	8 (24.2%)	0.82
Alcohol score	3.44	4.65	NA
TRISS score	0.89	0.81	0.15

Note. CIWA = Clinical Institute Withdrawal Assessment for Alcohol; TRISS = trauma and injury severity score.

Results

During the entire study period, 61 patients met inclusion criteria. Patient characteristics of each group are summarized in Table 2. Baseline characteristics of the 2 groups were similar in terms of gender and alcohol withdrawal as determined by the initiation of the Clinical Institute Withdrawal Assessment for Alcohol (CIWA) protocol. The intervention group had more elderly patients (≥ 65 years of age) than the preintervention group (10 patients, 31% vs 5 patients, 18%). The intervention group had a higher predicted mortality compared with the preintervention group defined from the baseline TRISS score, but that was not statistically significant (0.81 vs 0.89, $P = .15$).

There was no difference found in the incidence of delirium (33.3% vs 24.1%, $P = .45$), ICU LOS (10.11 vs 7.55 days, $P = .26$), ventilator duration (7.11 vs 5.03 days, $P = .26$), and mortality (7% vs 24.2%, $P = .07$) between the preintervention and intervention group (Table 3). Five patients, 1 in the preintervention group and 4 in the intervention group did not have documented CAM-ICU scores. Those patients were not included in the calculated delirium percentage. All of the deaths in both groups were from nondelirium-related causes (Table 4). Two patients were not able to be evaluated with the CAM-ICU assessment due to being unarousable and they were removed from the final calculation in the incidence of delirium. Hospital LOS was significantly shorter in the intervention group compared with the preintervention (9.83 vs. 14.75 days, $P = .04$). There was a significant reduction in the amount of anticholinergic medications ordered for the intervention group (15.2% vs 42.9%, $P = .016$). There was no difference found in the use of benzodiazepines (75% vs 63.3%, $P = .34$) and antipsychotics (42.9% vs 24.2%, $P = .12$) in the preintervention group compared with the intervention group.

Recommendations made by the pharmacists were recorded in the intervention group (Table 5) as a result of a CDSS alert. Forty-nine pharmacy interventions were made for the 33 intervention patients, with 46 (95%) of them accepted. There were 10 different categories that interventions fell into: (1) discontinuation of continuous sedation, (2)

Table 3. Patient Outcomes.

	Preintervention (n = 28, 27 ^a)	Intervention (n = 33, 29 ^a)	P value
Delirium present (CAM-ICU)	9 (33.3%) ^a	7 (24.1%) ^a	0.45
Average ICU LOS, days	10.11	7.55	0.26
Average hospital LOS, days	14.75	9.83	0.04
Average ventilator duration, days	7.11	5.03	0.26
All cause mortality	2 (7%)	8 (24.2%)	0.07
No. of delirium-potentiating medications			
Benzodiazepines	21 (75%)	21 (63.6%)	0.34
Anticholinergics (patients ≥ 65 years)	12 (42.9%)	5 (15.2%)	0.016
Antipsychotics	12 (42.9%)	8 (24.2%)	0.12

Note. CAM-ICU = Confusion Assessment Method for Intensive Care Unit; ICU = intensive care unit; LOS = length of stay.

^aThose patients who had no documented CAM-ICU scores were removed from the incidence of delirium calculation.

Table 4. Causes of Death.

Cause	Preintervention (n = 2)	Intervention (n = 9)
Endocarditis	1	0
MVC with internal injuries	1	0
Hemothorax with acute multifocal ischemic stroke	0	1
Intracranial hemorrhage	0	1
Cardiopulmonary failure	0	1
Cardiac arrest	0	1
Congestive heart failure	0	1
Subdural hematoma	0	2
Pulmonary embolism	0	1

Note. MVC = Motor vehicle collision.

Table 5. Pharmacists Interventions.

Pharmacist intervention	No. (%)
Discontinue continuous sedation	13 (27)
Discontinue sedating agent	12 (24)
Analgesic optimization	9 (18)
Laboratory monitoring	6 (12)
Decreased sedation rate	4 (8)
Changed sedating agent	4 (8)
Restarted home psychiatric meds	3 (6)
Discontinue stimulant	2 (4)
Increase sedation rate	1 (2)
Added sedative agent	1 (2)

discontinuation of sedating medications (benzodiazepines, opioids, anticholinergics), (3) analgesic optimization, (4) laboratory monitoring, (5) decreasing the sedation rate, (6) changing sedating agent, (7) restarting home psychiatric

medication(s), (8) discontinuation of stimulant(s), (9) increasing sedation rate, and (10) adding a sedating agent.

Discussion

The current study compared the impact of pharmacist monitoring with a CDSS on clinical outcomes related to ICU delirium.

With the addition of a CDSS, patients had a shorter hospital LOS and decreased administration of anticholinergic medications. Although there was no significant difference found in the incidence of delirium, ICU LOS, ventilator duration, benzodiazepines, and antipsychotic use, there was a decreasing trend observed in the intervention group. With pharmacists providing daily monitoring for at-risk patients and communicating potential issues with the multidisciplinary team during rounds, this likely contributed to a cultural change for ICU delirium-potentiating medications. After the implementation of CDSS rules with pharmacists monitoring, there was a decrease in the amount of benzodiazepines, antipsychotics, and anticholinergic medications ordered for patients in the TICU. Along with monitoring for appropriate use of these medications, pharmacists communicated with the treatment team the potential risk and paradoxical reactions of these medications used to treat the symptoms of delirium.

There was a nonsignificant increase in mortality rate in the intervention group compared with the preintervention (24.4% vs 7%, $P = .07$). No patient deaths were attributed to the presence of delirium or medications associated with delirium (Table 4). Because this study took place in the TICU, these patients had typically high acuity with multiple comorbidities. The TRISS scores are calculated on admission to the TICU, which provide a standard approach to predict the outcome in trauma cases. The intervention group had a higher trend of predicted mortality compared with the preintervention group defined from the baseline TRISS score, although this was not a statistically significant relationship (0.81 vs 0.89, $P = .15$). In future studies, in addition to TRISS scores, injury severity scores for trauma patients would be a beneficial baseline characteristics to examine. The possibility of the shorter hospital LOS due to patient loss was examined. For the patients with mortality, the average LOS was 7.4 vs 19 days in the intervention and preintervention, respectively. The patient loss in the intervention group would have influenced the outcome of LOS, favoring the postintervention group. With a larger sample size, we would anticipate that patient loss from nondelirium causes would be similar in each group.

The most common pharmacist intervention made was discontinuation of sedating medications, such as benzodiazepines, opioids, or anticholinergics. The Society of Critical Care Medicine guidelines have recognized that benzodiazepines and opioid use can contribute to the development of delirium.³ On the daily multidisciplinary rounds, along with CDSS utilization, the monitoring pharmacists would recommend judicious use of sedating medications.

There were several limitations to the current study. The relatively short duration of the study (45 days for each group) may have contributed to a lack of statistical significance in the primary outcome measure. This short duration also led to an inadequate number of patients for appropriate statistical analysis leading to an underpowered study. With the current study not reaching power, there is the possibility of a type II error. Extending the studies duration would capture a larger study population and likely adequately power the study. Another potential limitation was the reliance on nurse documentation of RASS and CAM-ICU scores leading to the possibility of variability in monitoring and documentation methods. The assumption had to be made that the scores were completed correctly as well. As noted in the results, 5 patients were not included for the calculation of delirium present due to undocumented CAM-ICU score. The study population was trauma, which is a specialty population, and the results may not be applicable to general ICU populations. All ICU patients are complicated and the trauma population experience different critical care scenarios that may not be applied to all types of ICUs. The CDSS rules would need to be expanded to different types of ICU areas to apply these results to the general ICU population and not just the TICU.

There were also limitations within the CDSS. Although this is an advanced CDSS that is able to link eMARs and laboratory data to one interface, not all of the pertinent data streams transfer to the system at this time. Patient RASS and CAM-ICU scores were manually extracted for each patient. For the ≥ 12 mg of lorazepam equivalents in 2 hours rule, the system could not discriminate between multiple doses of benzodiazepines or a titratable drip that was scanned. Adding additional rules to examine benzodiazepine doses over a 24-hour period, patients with CAM-ICU screenings who are positive for delirium and RASS scores less than -4 may enhance the future study results.

With the implementation of the CDSS rules, we observed a trend of decreasing rates of delirium, mechanical ventilation duration, ICU LOS, and potentiating medication use. Going forward, incorporating CDSS rules into the pharmacist daily workflow could be beneficial for patient outcomes. A longer study duration with more patients would be required to determine the possible benefit of the CDSS rules before adding CDSS developed rules into pharmacist's workflow. Future work with CDSS delirium monitoring would examine focus on the length of time that patients spent on the ventilator and time spent within goal RASS. These outcomes would show if the CDSS alerting in real times leads to timely intervention and reduction in ICU delirium.

Conclusion

For patients admitted to the TICU receiving continuous sedation and delirium-potentiating medication, the use of CDSS rules with daily pharmacist's intervention and monitoring reduced hospital LOS and use of anticholinergic medications. Future studies could be beneficial in determining the full impact of CDSS on ICU-related delirium.

Appendix

Continuous Sedation Intervention:

Escalating Doses of Benzodiazepine Interventions:

Delirium Potentiating Medication Interventions:

Targets of CDSS and standardized pharmacists intervention.

Note. CDSS = clinical decision support system; RASS = Richmond Agitation Sedation Scale; CAM-ICU = Confusion Assessment Method for Intensive Care Unit; DC = Discontinue.

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